Office Action Summary	Application No. 09/269,874	Applicant(s) Bujard
	Examiner Patricia A. Duffy	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 5, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *42-82* is/are pending in the application.

4a) Of the above, claim(s) *50-52 and 58-82* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *42-49 and 53-57* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *42-48* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment and responses filed 11-20-01, 2-28-03, 3-11-03 and 6-5-03 have been entered into the record. Claims 42-82 are pending, claims 42-49 and 52-57 are pending and under examination.

2. Any rejection not maintained herein is withdrawn based on Applicants' arguments.

Priority

3. Receipt is acknowledged of foreign priority papers from WIPO submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

4. The drawings are objected to for the reasons set forth on the enclosed PTO-948. A proposed drawing correction or corrected drawings are required in reply to this Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

5. The disclosure is objected to because of the following informalities: the specification at least pages 7 and 10, the text references a claim number. Since claims may be canceled or changed upon allowance, references to a claim number is not permissible in the text of the specification. Applicants should review the specification for additional references to claim numbers. Applicants are cautioned against adding new matter into the specification and the inserted material should correspond exactly to the text of the original claims that they referenced.

Appropriate correction is required.

Claim Objections

6. Claims 47, 48 and 49 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim requires production of the "complete" gp190/MSP1 from a *Plasmodium* and the complete gp190 protein as disclosed contains both an attachment signal and a signal peptide. Therefore, these limitations are already included in polypeptide of claim 42. Further, claim 49 is directed to specific fragments of gp190 and as such broadens the scope of the claim from which it depends.

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 42-49 and 53-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As to claims 42-49 and 53-57, the claims recite that the AT content of the expressed nucleotide sequence encoding the complete gp190/MSP1 protein is less that of the AT content of "a" naturally occurring nucleotide sequence encoding "a" gp190/MSP1 protein. This claim reads on a reduction of any AT content in any MSP1 nucleotide sequence as compared to any other naturally occurring sequence. It is noted that the specification provides support, only for a reduced AT content compared to the corresponding naturally occurring MSP1 nucleotide sequence from which it is derived. As such, conception of the comparison of the reduced AT content nucleotide sequence with any and all naturally occurring nucleic acid sequences encoding any gp190/MSP1 protein is not provided for in this specification.

As to claims 47 and 48, the claims are drawn to a method of producing a compete gp190/MSP1 polypeptide from a *Plasmodium* comprising expression a nucleotide sequence encoding the protein in a single expression vector wherein the AT content of the expressed nucleotide sequence is less than the AT content of a naturally occurring nucleotide sequence encoding a gp190/MSP1 polypeptide wherein the nucleotide sequence further comprises and attachment signal or further comprises a signal peptide. While the specification provides for expression of fragments lacking the attachment signal or signal peptide (pages 7-8) and these fragments further comprising the attachment signal or signal peptide, *the specification fails to provide for these additional sequences attached to the complete sequence which already has these sequences present.* As such, a complete nucleotide sequence further comprising these sequences lacks conception by way of written description in the specification as originally filed.

These issues are best resolved by pointing to the specification by page and line number were written description support for the claimed subject matter can be found.

10. Claims 42-49 and 53-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to methods of producing gp190/MSP1 proteins from the genus *Plasmodium* using a nucleotide sequences that is reduced in its adenine-thymine content as compared to a naturally occurring gp190/MSP1 nucleotide sequence. The specification discloses a single nucleotide sequence from *Plasmodium falciparum*. The claims encompass modified sequences from other Plasmodium species such as *P. vivax, P. ovale* and *P. malariae*. there is at least 100 different species of Plasmodium. The specification fails to describe the complete nucleotide sequences encoding the naturally occurring gp190/MSP1 proteins corresponding to a representative number of these other species, sufficient to describe the genus of nucleotide sequences that are modified to produce nucleotide sequences that are "reduced" in their adenine-thymine content. Conception and written description of these sequences are required in order to produce the claimed nucleotide sequence that has a reduced adenine-thymine content in order to produce the "complete" gp190/MSP1 protein. In order to produce the polypeptide recombinantly, the corresponding nucleic acid with reduced AT content is required. The specification discloses a single native nucleotide sequence (SEQ ID NO:2) that is modified to produce a sequence that has a reduced adenine-thymine content. The specification fails to disclose any nucleic acid sequence that encodes an isolated polypeptide of any other gp190/MSP1 said polypeptide has all the properties of the gp190/MSP1 of *P. falciparium*. The teachings of the specification are limited to amino acid sequence comprising SEQ ID NO:1 and 2 which correspond to the naturally occurring nucletide sequence encoding gp190/MSP1 polypeptide and the nucleotide

sequence that has a reduced adenine-thymine content. The nucleic acids sequence encoding these specific protein of SEQ ID NO:3 have written description. However, the claims encompass nucleic acids from other *Plasmodium* species, unlimited variants and fragments (see definition of "complete" on page 6, fifth full paragraph). The disclosure of a single naural and modified nucleic acid encoding the same polypeptide does not provide written description support for conception and possession of the genus now claimed, because a represnetaive number of naurally occurring (i.e. native) and adenine-thymine reduced (i.e. modified) nucleic acid sequences have been provided, such that the skilled artisan would not recognize that Applicants were in possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of a nucleotide sequence with reduced adenine-thymine content as compared to SEQ ID NO:1 and encoding the polypeptide of SEQ ID NO:3, the skilled artisan cannot envision the detailed chemical structure of the encompassed nucleotide sequences that are used to produce the undescribed proteins of other at least 100 Plasmodium species and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. This specification fails to provide a description of a complete nucleic acid or complete protein sequence for a representative number of species that fall within the claimed genus. As such, the specification lacks written description for a generic method of producing the "complete" gp190/MSP1 from the genus *Plasmodium* using a nucleotide sequence that has reduced AT content. recombinant polypeptide or generic recombinant polypeptide fragments.

11. Claims 53 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection is mainatined for reasons made of record in Paper No. 22, mailed 11-20-01.

Applicants argue that the plasmids were publically available. This is not persuasive, Hochuli et al do not teach the claimed dPS56RBSII. The claimed plasmid is not referenced in this document. Similarly, Bujiard et al, does not teach this claimed plasmid. It is noted that the plasmide of Hochuli is not described as the claimed plasmide and the construction of the plasmid is not fully disclosed becuse it uses undisclosed sequences (i.e. a regulatable promotor/operator) that is unpublished.Applicants alledget hat pBI-5 was disclosed in Baron et al. This is not persuasive, there is no named or described plasmide in any figure or test that is pBi-5. With respect to the Ph.D. Thesis of Ivana Turbachova, this is not persuasive because it is not in the English language and therefore can not be evaluated. Further, it is also not persuasive because it does provide for any information to indicate that the claimed plasmid was in the prior art at the time that the invention was made. Finally, none of the provided references teach the nucleotide sequence of the claimed plasmids. The evidence

with respect to the particular named strain of *E. coli*, DH5αZ1 is not persuasive, because the method of Lutz et al depends on *E. coli* strain DH5αpLDR8 that is not described and not publically available in any Patent Depository or described therein. Applicants argue that the choice of the vector or bacterial strain was not part of the invention. This is not persuasive, the claims recite specific vectors and bacterial strains and as such clearly, the choice of vector and bacterial strain are claimed and therefore specifically part of the claimed invention. Applicants argue that the FCB-1 strain of Plasmodium falciparum is disclosed in Miller et al (Molecular Biochemical Parasitology, 59:1, 1993; Exhibit 6). This is not persuasive because the claimed invention is not drawn to this sequence and Miller et al discloses polypeptide sequences and not nucleic acid sequences. Further, there is no sequence in Miller et al that is noted "FCB-1" as argued by Applicants. Therefore, the relevance of this argued evidence is not clear.

12. Claims 42-49 and 53-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 42-49 and 53-57, the claims recite the term "a nucleotide encoding the complete gp910/MSP-1 protein". While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "complete" in the claim is used conventionally in the claim to mean the full-length protein and the corresponding full-lenght nucleic acid. However, the "complete gp190/MSP-1 protien" as specifically defined in the specification at page 6 to mean the enteire gp190/MSP1 surfact protein isolatable from the above named Plasmodia, especially *Plasmoidum falciparum*, representing the main surface protein of the above named parasite as well as the protein with analgous function from the other Plasmodium species such as *P. vivax*. The term therefore comprises in each case the

main surface protien of the merozoites of the four malaria parasites named above as dangerous to man. "Complete gp190/MSP1 gene" means the gene coding for this protein. In this contest "complete" signifies that the entire amino acid sequence of the native protein is present or that the gene sequence codes for the entire amino-acid sequence of the native protien. *Mutated and/or shortened forms of pg190/MSP1 are however included therewith insofar as they display the same immunization poteintial (vaccine protection) as the complete gp190/MSP1 [emphasis added].*" Thus, this definition of complete as set forth in the specificaiton at page 6, specifically includes mutated or shortened forms. Such, shortened forms are not "complete" because the accepted meaning is "the eitirity of an entity", "total or absolute" and not parts thereof or mutants thereof. Applicants "redefinition" of the conventional meaning of complete in the specificaiton to include parts and mutants is repugnant to the convential meaning of "complete".

As to claim 42 and every claim dependent thereon, the claims are rendered indefinite because it presents a comparison of two sequences wherein the "naturally occuring nucleotide sequence" is not structurally defined and therefore, the metes and bounds of any sequence to be compared can not be ascertained.

As to claim 46, the claim is indefinite in the recitation of wherein the nucleotide sequence encoding the complete gp190/MSP-1 is set forth in SEQ ID NO:2 because there are at least two nucleotide sequence in claim 42, the "naturally occurring" and one possessing the reduced adenine and thymine content. As such, the antecedent basis for this sequence is unclear.

Claim Rejections - 35 USC § 102 or 103

13. Claims 42-48 and 54 stand rejected under 35 U.S.C. 102(b) as being anticipated or under 35 U.S.C. 103(a) as being unpatentable over Holder et al (Nature, 317:270-273, 1985).

Holder et al teach the production of specific fragments of the full length pg190/MSP1 from Plasmodium falciparum (see page 272, paragraph bridging columns 1-2). It is noted that each of the fragments was produced in a single vector as claimed. It is further noted that the definition of "complete" in the specification at page 6, specifically includes such fragments and variants and does not define the specific sequence that it is "reduced". As such, the gp190/MSP-1 fragments expressed in a single vector in *E. coli* as taught by holder inherenly possess less adenine-thymine content than the naturally occurring full length gene of *Plasmodium falciparum* shown in Figure 2 taught by Holder et al.

Applicants arguments have been carefully considered but are not persuasive. Applicants argues that Holder et al teaches fragments. This is not persuasive, Applicants definition of "complete" on page 6 of the specification is inclusive of "shorter forms". Applicants argue that the AT content of the sequence encoding of the protein of Holder et al is not less than that of a naturally-occurring sequence. This is not persuasive because the fragment by definition has less AT-content than the full-length naturally occurring sequence. The claims do not define the specific sequence for comparison. The claims do not define the lenght of the sequence, merely that is must be "any" or "a" naturally occurring sequence. The claims do not require the "corresponding" naturally occuring sequence. The reciation of "a" has been interpreted as "any". Applicants are arguing definitions and limitations that are contradictory to how the specification defines these terms and are not in the claims.

The rejection is maintained across the recited claims.

Status of Claims

14. No claims are allowed. All claims stand rejected.

15. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
August 24, 2003

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600